MICROCIRCULATION AND TARGET ORGAN DAMAGE IN RHEUMATIC AND SKIN DISEASES

RELEASE DATE: November 25, 2002

RFA: AR-03-005

National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
(http://www.niams.nih.gov)
National Eye Institute (NEI)
(http://www.nei.nih.gov/)
Office of Research on Women's Health (ORWH)
(http://www4.od.nih.gov/orwh/)

LETTER OF INTENT RECEIPT DATE: February 10, 2003

APPLICATION RECEIPT DATE: March 20, 2003

THIS RFA CONTAINS THE FOLLOWING INFORMATION

PURPOSE OF THIS RFA

The National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Eye Institute (NEI) and the Office of Research on Women's Health (ORWH) invite applications to address the mechanisms of end organ damage and alterations in the microcirculation in rheumatic and autoimmune skin diseases. This initiative has three primary purposes. The first purpose is to promote research targeted towards identification and evaluation of cellular, molecular and genetic pathways involved in target organ damage and altered microcirculation in rheumatic and skin diseases. The second purpose of this request for applications is to stimulate and encourage: a) innovative and multidisciplinary basic, translational and clinical studies and b) discovery research projects using new technologies (e.g. microarrays, high throughput sequencing, multi-color flow cytometry, differential display, proteomics, etc). Finally, the purpose of this initiative is to encourage applications as collaborations or as research teams combining interdisciplinary approaches between autoimmune disease researchers and experts in other related scientific fields, such as nephrology and neurology, and vascular biology. The applications in response to this RFA may be for individual research projects (R01) or for exploratory/developmental grants (R21). This RFA solicits basic, translational, and clinical research projects but not epidemiological or clinical treatment projects.

RESEARCH OBJECTIVES

Background

Although immune dysregulation plays a major role in the induction of autoimmunity, recent evidence suggests that structural and functional properties of target/end organs, such as eyes, kidneys, synovium, skin, thyroid gland, and islet cells, may contribute significantly to the development of tissue damage and clinical disease. In animal models, a variable threshold to renal and cardiac damage has been clearly demonstrated. This finding is consistent with clinical observations showing that individuals with the same serologic abnormality do not necessarily have the same tissue abnormality. Some of the deleterious effects of autoreactivity are likely due to interactions between autoantibodies and specific cellular elements in the target organ beyond the activation of the complement cascade. For example, autoantibodies may bind to cell surface receptors and trigger cell activation, modify cell function, or induce apoptosis. Further, the type of interaction may influence clinical expression. In lupus nephritis, immunoglobulins produce distinguishable deposit patterns in specific glomerular locations and this is associated with different disease profiles. The differences appear to be based on the differential reactivity of the autoantibodies with specific glomerular antigens, suggesting that antigen display in the target organ influences tissue damage.

Recent advances indicate that other end organ processes may be related to the induction and maintenance of damage in the context of rheumatic and autoimmune skin diseases. These include expression of proteins related to organ development, either spontaneously or induced by the cytokine milieu created by the inflammatory response, events related to single cell death during organ development and repair, and newly identified binding properties of autoantibodies present in sera from patients with autoimmune diseases that trigger apoptosis, cell activation or block binding of the natural ligand.

Vulnerability of the target organ to immune-mediated damage also appears to be genetically determined. In fact, the genetic mapping of susceptibility genes in diabetes and lupus suggests an important role for the target organ in the induction of tissue injury, with contributions made by the cellular components and their interactions with the extracellular matrix, independent of other known factors such as HLA. For example, in murine models of systemic lupus, nephritis is differentially induced in different strains of mice, in spite of similar autoantibody profiles and in the presence of similar T-cell reactivity. Recent data from genetic analysis of backcrosses of autoimmune- disease-prone mice in a model of autoimmune myocarditis also suggest that genetic factors unrelated to immune-related susceptibility loci are important in the development and severity of symptoms.

The vasculature is often a direct target of autoimmune damage. End organ damage may be secondary to primary damage to the vasculature in some cases, or vascular damage and compromised circulation may further contribute to target organ damage. Indeed, the microcirculation has been shown to be involved in the pathogenesis and target organ damage in several rheumatic diseases. Scleroderma is fraught with microvascular alterations resulting in general changes in vasoreactivity as seen in Raynaud's syndrome, as well as decreased angiogenesis. On the other hand, increased angiogenesis is seen in rheumatoid arthritis and skin manifestations of lupus. Increased levels of angiogenic growth factors may be a biomarker for ankylosing spondylitis. The immune complex deposition and thrombotic events leading to stroke and myocardial infarction in systemic lupus erythematosus (SLE, lupus) occur in the microcirculation. Where the microcirculation lies in the cause and effect of rheumatic diseases is unclear, but its involvement warrants study.

In recent years, knowledge of angiogenesis and the microcirculation has dramatically increased, as has the ability to manipulate genetic material and cell behavior. Several aspects of angiogenesis have undergone substantial growth and development and, in a parallel fashion, several new technologies and methodologies have been applied to the study of the cells that make up the microcirculation, endothelial cells, pericytes and smooth muscle cells. Insights into

mechanisms associated with embryonic development, cancer, and vascular remodeling during injury or inflammation could have a strong impact on rheumatic and skin diseases. For example, integrins, growth factors, chemokines and/or inflammatory cytokines as well as receptors for any of them, are all current targets for therapeutic blockers of inflammation. Angiostatins, found to be effective in starving tumors of their blood supply, are now in clinical trials for cancer patients. In addition, gene therapies are being developed for constitutive or inducible production of a particular protein for systemic or tissue specific application. Previous results have shown that angiogenesis inhibitors may delay or prevent onset of experimental arthritis in mice and rats. Preliminary work is underway to identify angiogenesis inhibitors for use in humans with rheumatoid arthritis (RA). Therefore, the application of current concepts in vascular biology to the study of rheumatic and autoimmune skin diseases may provide new insights into disease progression and expand the therapeutic options.

Scope

The focus of the studies is to be on the immune and nonimmune mechanisms of induction and development of injury, and dissection of the genetics, of microcirculation and end organ involvement in the context of rheumatic and autoimmune skin diseases. Relevant rheumatic diseases covered under this RFA include but are not limited to lupus, rheumatoid arthritis, scleroderma, dermatomyositis, vasculitis, juvenile rheumatic diseases and Sjogren's syndrome, as well as ocular manifestations of rheumatic diseases (e.g. uveitis, retinopathy).
Relevant skin diseases include but are not limited to psoriasis, atopic dermatitis, autoimmune bullous diseases, alopecia areata, vitiligo and vasculitis. Knowledge gained by research in this area will make it possible to construct a more comprehensive picture of disease pathogenesis. Definition of discrete pathogenic processes involving the target organs may provide the scientific rationale for new forms of interventions.

Appropriate research areas may include, but are not limited to, the following:

o Development and evaluation of new experimental systems, including the generation of transgenic and other genetically engineered animal models, to study cellular, molecular, and genetic aspects of target organ involvement.

o Development of new in vitro models to analyze the effects of inflammatory, immune, and other mechanisms of injury on target organ/cell function and structure.

o Identification and characterization of cellular and molecular pathways involved in target/end organ damage.

o Mechanistic studies on the initiation and perpetuation of local immune and inflammatory responses that occur in organs involved in autoimmune diseases.

o Mechanistic studies of sex differences in susceptibility and severity of altered microcirculation and end organ damage in autoimmune diseases.

o Studies on the changes in target organ structure and function due to the presence of local immune, inflammatory, and other forms of tissue injury related to autoimmune disease.

o Studies of the effects of immune and nonimmune mechanisms of tissue damage and their effects on target organ cell structure and function.

o Studies on the effects of autoreactive or other relevant immune or inflammatory responses on target/end organ repair processes.

o Studies of mechanisms underlying phenotypic changes in cellular components of target organs during different phases of disease.

o Identification of biochemical, structural, or other markers that may correlate with early, preclinical target organ involvement and that may predict disease progression or severity.

o Studies to identify mediators and mechanisms that may protect target organs from the inflammatory, immune, and other forms of tissue injury involved in rheumatic and skin diseases.

o Immediate and long term effects on the microvascular function of antibody therapy for rheumatic and skin diseases.

o Molecular approaches to affect vascular dysfunction in rheumatic diseases, such as use of angiostatins or angiogenic factors.

o Targeting molecules involved in maintaining vascular structure and function for local or systemic therapy using gene therapy and other pharmacologic interventions (constitutive or inducible) in rheumatic and skin diseases.

o Translational research aimed at correlating clinical findings with markers of end organ damage.

o New methodologies to facilitate studies of gene expression and characterization of the phenotype of involved tissues.

o Application of new genetic, molecular, biochemical, imaging or bioinformatics methodologies to the study of end organ damage and its manifestations.

This list is intended to be illustrative and not exclusive or restrictive.

MECHANISM OF SUPPORT

This RFA will use the NIH Research Project Grant (R01) and the Exploratory/Developmental Research Project (R21). As an applicant you will be solely responsible for planning, directing, and executing the proposed project. This RFA is a one-time solicitation. Future unsolicited, competing-continuation applications, based on this project will compete with all investigator-initiated applications and will be reviewed according to the customary peer review procedures. The anticipated award date is September 30, 2003.

This RFA uses just-in-time concepts. It also uses either the modular or the non-modular budgeting formats (see http://grants.nih.gov/grants/funding/modular/modular.htm). Specifically, if you are submitting an application with direct costs in each year of $250,000 or less, use the modular format. Otherwise follow the instructions for non-modular research grant applications.

R01 Applications: An R01 applicant may request a project period of up to 4 years and a budget for direct costs not to exceed $500,000 per year.

R21 Applications. The R21 application may request a project period up to two years with a budget not to exceed $100,000 per year in direct costs, not including indirect costs for collaborating institutions, if any.

The R21 projects solicited under this RFA are exploratory/developmental grants. In the context of this RFA, exploratory/ developmental grants are to be used to either a) gather preliminary data to develop a research basis for a subsequent application through other mechanisms,

i.e., R01, P01, or b) to explore the feasibility of an innovative or conceptually creative research question or approach that may not be justifiable through existing research to compete as a standard research project grant (e.g., R01). Because innovative projects may require a preliminary test of feasibility, the R21 mechanism could provide short-term support for such preliminary work. Exploratory/developmental studies are not intended for large-scale undertakings, nor are they intended to support or supplement ongoing research.

Investigators with expertise in the physiology, pathology, and genetics of organs and tissues involved in rheumatic, skin, and autoimmune diseases who wish to establish research programs in the context of autoimmune diseases are encouraged to apply. Also encouraged are investigators with expertise in immune mechanisms of disease and autoimmunity who wish to expand their research to mechanisms of target organ damage.

FUNDS AVAILABLE

The estimated total funds (direct and facilities and administrative (F&A) costs) available for the first year of support for all awards made under this RFA will be $3,250,000. Because the nature and scope of the proposed research will vary from application to application, it is anticipated that the size and duration of each award will also vary. Although the FY 2003 financial plans of the NIAMS provide support for this program, awards pursuant to the RFA are contingent upon the availability of funds and the receipt of a sufficient number of meritorious applications. At this time, it is not known if this RFA will be reissued.

ELIGIBLE INSTITUTIONS

You may submit an application if your institution has any of the following characteristics:

- For-profit or non-profit organization
- Public or private institutions such as universities, colleges, hospitals, and
- Laboratories
- National laboratories
- Units of state and local governments
- Eligible agencies of the Federal government
- Domestic or foreign

INDIVIDUALS ELIGIBLE TO BECOME PRINCIPAL INVESTIGATORS

Any individuals with the skills, knowledge, and resources necessary to carry out the proposed research are invited to work with their institutions to develop an application for support. Individuals from underrepresented racial and ethnic groups as well as individuals with disabilities are always encouraged to apply for NIH programs.

WHERE TO SEND INQUIRIES

We encourage inquiries concerning this RFA and welcome the opportunity to answer questions from potential applicants. Inquiries may fall into three areas: scientific/research, peer review, and financial or grants management issues:
o Direct your questions about scientific/research issues to:

J. Elizabeth Gretz, Ph.D.
Director, Immunology and Inflammation Program
Rheumatic Diseases Branch, NIAMS, NIH
One Democracy Plaza
6701 Democracy Boulevard, Suite 800, MSC 4872
Bethesda, MD 20872-4872
Telephone: (301) 594-5032
FAX: (301) 480-4543
Email: gretze@mail.nih.gov

Alan Moshell, M.D.
Director, Skin Diseases Program, NIAMS, NIH
One Democracy Plaza
6701 Democracy Boulevard, Suite 800, MSC 4872
Bethesda, MD 20872-4872
Telephone: (301) 594-5017
FAX: (301) 480-4543
Email: moshella@mail.nih.gov

Richard S. Fisher, Ph.D.
Director, Corneal Diseases Program
Division of Extramural Research
6120 Executive Blvd, MSC 7164 Bethesda, MD 20892-7164
National Eye Institute, NIH
Executive Plaza South, Suite 350

Bethesda, MD 20892-7164
(For FEDEX use: Rockville, MD 20852)
FAX: 301-402-0528
Telephone: 301-451-2020
Email: cornea@nih.gov

Lisa Begg, Dr.P.H., R.N.
Director of Research Programs
Office of Research on Women's Health
Office of the NIH Director, NIH
Building 1, Room 201
9000 Rockville Pike
Bethesda, MD 20892-0161
Telephone: 301/402-1770
FAX: 301/402-1798
Email: beggl@od.nih.gov

o Direct your questions about peer review issues to:

Tracy Shahan, Ph.D.
National Institute of Arthritis and Musculoskeletal and Skin Diseases
One Democracy Plaza
6701 Democracy Boulevard, Suite 800, MSC 4872
Bethesda, MD 20872-4872
Telephone: (301) 594- 4952
FAX: (301) 402- 2406
Email: shahant@mail.nih.gov

o Direct your questions about financial or grants management matters to:

Mr. Michael G. Morse
Deputy Grants Management Officer
National Institute of Arthritis and Musculoskeletal and Skin Diseases
One Democracy Plaza
6701 Democracy Boulevard, Suite 800, MSC 4872
Bethesda, MD 20872-4872
Telephone: (301) 594-3535

FAX: (301) 480- 5450
Email: morsem@mail.nih.gov

William W. Darby
Grants Management Officer
Division of Extramural Research
National Eye Institute Executive Plaza South, Suite 350
6120 Executive Blvd, MSC 7164 Bethesda, MD 20892-7164
Telephone: (301) 496-5884
FAX: (301- 496-9997
Email: wwd@nei.nih.gov

LETTER OF INTENT

Prospective applicants are asked to submit a letter of intent that includes the following information:

- Descriptive title of the proposed research
- Name, address, and telephone number of the Principal Investigator
- Names of other key personnel
- Participating institutions
- Number and title of this RFA

Although a letter of intent is not required, is not binding, and does not enter into the review of a subsequent application, the information that it contains allows NIAMS staff to estimate the potential review workload and plan the review.

The letter of intent is to be sent by the date listed at the beginning of this document. It is preferred that the letter of intent be sent electronically. If necessary, the letter of intent can be sent by regular mail. The letter of intent should be sent to:

J. Elizabeth Gretz, Ph.D.
Director, Immunology and Inflammation Program
Rheumatic Diseases Branch, NIAMS, NIH
One Democracy Plaza
6701 Democracy Boulevard, Suite 800, MSC 4872
Bethesda, MD 20872-4872

Telephone: (301) 594-5032
FAX: (301) 480-4543
Email: gretze@mail.nih.gov

SUBMITTING AN APPLICATION

Applications must be prepared using the PHS 398 research grant application instructions and forms (rev. 5/2001). The PHS 398 is available at http://grants.nih.gov/grants/funding/phs398/phs398.html in an interactive format. For further assistance contact GrantsInfo,
Telephone (301) 435-0714,
Email: GrantsInfo@nih.gov.

SUPPLEMENTAL INSTRUCTIONS:

RESEARCH PLAN - The research plan (a-d) is limited to 25 pages for R01 applications and 10 pages for R21 applications. Applications that exceed the page limit will be returned without review. An appendix may be included in the application; however, the appendix is not to be used to circumvent the page limit of the research plan.

For the R21 application, preliminary data supporting feasibility of approach are not required, however, if included, the section may not exceed 1 page. In addition, a paragraph should be included in the Significance section of the application that specifies either how the project presents a new direction for the work performed in the PI's laboratory or the innovative nature of the research question or approach, and how it may advance the understanding of the mechanisms of target organ damage or altered microcirculation in rheumatic and autoimmune skin diseases.

SPECIFIC INSTRUCTIONS FOR MODULAR GRANT APPLICATIONS: Applications requesting up to $250,000 per year in direct costs must be submitted in a modular grant format. The modular grant format simplifies the preparation of the budget in these applications by limiting the level of budgetary detail. Applicants request direct costs in $25,000 modules. Section C of the research grant application instructions for the PHS 398 (rev. 5/2001) at http://grants.nih.gov/grants/funding/phs398/phs398.html includes step-by-step guidance for preparing modular grants. Additional information on modular grants is available at http://grants.nih.gov/grants/funding/modular/modular.htm.

USING THE RFA LABEL: The RFA label available in the PHS 398 (rev. 5/2001) application form must be affixed to the bottom of the face page of the application. Type the RFA number on the label. Failure to use this label could result in delayed processing of the application such that it may not reach the review committee in time for review. In addition, the RFA title and number must be typed on line 2 of the face page of the application form and the YES box must be marked. The RFA label is also available at:
http://grants.nih.gov/grants/funding/phs398/label-bk.pdf

SENDING AN APPLICATION TO THE NIH: Submit a signed, typewritten original of the application, including the Checklist, and three signed,
photocopies, in one package to:

Center For Scientific Review
National Institutes of Health
6701 Rockledge Drive, Room 1040, MSC 7710
Bethesda, MD 20892-7710
Bethesda, MD 20817 (for express/courier service)

At the time of submission, two additional copies of the application must be sent to:

Tracy Shahan, Ph.D.
National Institute of Arthritis and Musculoskeletal and Skin Diseases
One Democracy Plaza
6701 Democracy Boulevard, Suite 800, MSC 4872
Bethesda, MD 20872-4872
Telephone: (301) 594-4952
FAX: (301) 402-2406
Email: shahant@mail.nih.gov

APPLICATION PROCESSING: Applications must be received by the application receipt date listed in the heading of this RFA. If an application is received after that date, it will be returned to the applicant without review.

The Center for Scientific Review (CSR) will not accept any application in response to this RFA that is essentially the same as one currently pending initial review, unless the applicant withdraws the pending application. The CSR will not accept any application that is essentially the same as

one already reviewed. This does not preclude the submission of substantial revisions of applications already reviewed, but such applications must include an Introduction addressing the previous critique.

PEER REVIEW PROCESS

Upon receipt, applications will be reviewed for completeness by the CSR and responsiveness by the NIAMS. Incomplete applications will be returned to the applicant without further consideration. And, if the application is not responsive to the RFA, NIAMS staff may contact the applicant to determine whether to return the application to the applicant or submit it for review in competition with unsolicited applications at the next appropriate NIH review cycle.

Applications that are complete and responsive to the RFA will be evaluated for scientific and technical merit by an appropriate peer review group convened by the NIAMS in accordance with the review criteria stated below. As part of the initial merit review, all applications will:

o Receive a written critique
o Undergo a process in which only those applications deemed to have the highest scientific merit, generally the top half of the applications under review, will be discussed and assigned a priority score
o Receive a second level review by an appropriate council or board

REVIEW CRITERIA

The goals of NIH-supported research are to advance our understanding of biological systems, improve the control of disease, and enhance health. In the written comments, reviewers will be asked to discuss the following aspects of your application in order to judge the likelihood that the proposed research will have a substantial impact on the pursuit of these goals:

o Significance
o Approach
o Innovation
o Investigator
o Environment

The scientific review group will address and consider each of these criteria in assigning your application's overall score, weighting them as appropriate for each application. Your application

does not need to be strong in all categories to be judged likely to have major scientific impact and thus deserve a high priority score. For example, you may propose to carry out important work that by its nature is not innovative but is essential to move a field forward.

(1) SIGNIFICANCE: Does your study address an important problem? If the aims of your application are achieved, how do they advance scientific knowledge? What will be the effect of these studies on the concepts or methods that drive this field?

(2) APPROACH: Are the conceptual framework, design, methods, and analyses adequately developed, well integrated, and appropriate to the aims of the project? Do you acknowledge potential problem areas and consider alternative tactics?

(3) INNOVATION: Does your project employ novel concepts, approaches or methods? Are the aims original and innovative? Does your project challenge existing paradigms or develop new methodologies or technologies?

(4) INVESTIGATOR: Are you appropriately trained and well suited to carry out this work? Is the work proposed appropriate to your experience level as the principal investigator and to that of other researchers (if any)?

(5) ENVIRONMENT: Does the scientific environment in which your work will be done contribute to the probability of success? Do the proposed experiments take advantage of unique features of the scientific environment or employ useful collaborative arrangements? Is there evidence of institutional support?

ADDITIONAL REVIEW CRITERIA: In addition to the above criteria, your application will also be reviewed with respect to the following:

o PROTECTIONS: The adequacy of the proposed protection for humans, animals, or the environment, to the extent they may be adversely affected by the project proposed in the application.

o INCLUSION: The adequacy of plans to include subjects from both genders, all racial and ethnic groups (and subgroups), and children as appropriate for the scientific goals of the research. Plans for the recruitment and retention of subjects will also be evaluated. (See Inclusion Criteria included in the section on Federal Citations, below).

o DATA SHARING: The adequacy of the proposed plan to share data.

o BUDGET: The reasonableness of the proposed budget and the requested period of support in relation to the proposed research.

OTHER REVIEW CRITERIA:

In addition to the above criteria, in accordance with NIH policy, all R21 applications will also be reviewed with respect to the following:

o In the context of this RFA, the R21 exploratory/developmental grants are to be used to either: a) gather preliminary data to develop a research basis for a subsequent application through other mechanisms, i.e., R01, P01, or b) explore the feasibility of an innovative or conceptually creative research question or approach that may not be justifiable through existing research to compete as a standard research project grant (e.g., R01).

o Preliminary data supporting feasibility of approach are not required.

RECEIPT AND REVIEW SCHEDULE

Letter of Intent Receipt Date: February 10, 2003
Application Receipt Date: March 20, 2003
Peer Review Date: July 2003
Council Review: September 2003
Earliest Anticipated Start Date: September 2003

AWARD CRITERIA

Award criteria that will be used to make award decisions include:

o Scientific merit (as determined by peer review).
o Use of interdisciplinary team/approaches.
o Availability of funds.
o Programmatic priorities.

REQUIRED FEDERAL CITATIONS

INCLUSION OF WOMEN AND MINORITIES IN CLINICAL RESEARCH: It is the policy of the NIH that women and members of minority groups and their sub-populations must be included in all NIH-supported clinical research projects unless a clear and compelling justification is provided indicating that inclusion is inappropriate with respect to the health of the subjects or the purpose of the research. This policy results from the NIH Revitalization Act of 1993 (Section 492B of Public Law 103-43).

All investigators proposing clinical research should read the AMENDMENT "NIH Guidelines for Inclusion of Women and Minorities as Subjects in Clinical Research - Amended, October, 2001," published in the NIH Guide for Grants and Contracts on October 9, 2001 (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-001.html); a complete copy of the updated Guidelines is available at http://grants.nih.gov/grants/funding/women_min/guidelines_amended_10_2001.htm.
The amended policy incorporates: the use of an NIH definition of clinical research; updated racial and ethnic categories in compliance with the new OMB standards; clarification of language governing NIH-defined Phase III clinical trials consistent with the new PHS Form 398; and updated roles and responsibilities of NIH staff and the extramural community. The policy continues to require for all NIH-defined Phase III clinical trials that: a) all applications or proposals and/or protocols must provide a description of plans to conduct analyses, as appropriate, to address differences by sex/gender and/or racial/ethnic groups, including subgroups if applicable; and b) investigators must report annual accrual and progress in conducting analyses, as appropriate, by sex/gender and/or racial/ethnic group differences.

INCLUSION OF CHILDREN AS PARTICIPANTS IN RESEARCH INVOLVING HUMAN SUBJECTS: The NIH maintains a policy that children (i.e., individuals under the age of 21) must be included in all human subjects research, conducted or supported by the NIH, unless there are scientific and ethical reasons not to include them. This policy applies to all initial (Type 1) applications submitted for receipt dates after October 1, 1998.

All investigators proposing research involving human subjects should read the "NIH Policy and Guidelines" on the inclusion of children as participants in research involving human subjects that is available at http://grants.nih.gov/grants/funding/children/children.htm.

REQUIRED EDUCATION ON THE PROTECTION OF HUMAN SUBJECT PARTICIPANTS: NIH policy requires education on the protection of human subject participants for all investigators submitting NIH proposals for research involving human subjects. You will find this policy announcement in the NIH Guide for Grants and Contracts Announcement, dated June 5, 2000, at

http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html.

HUMAN EMBRYONIC STEM CELLS (hESC): Criteria for federal funding of research on hESCs can be found at http://grants.nih.gov/grants/stem_cells.htm and at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-02-005.html.
Only research using hESC lines that are registered in the NIH Human Embryonic Stem Cell Registry will be eligible for Federal funding (see http://escr.nih.gov). It is the responsibility of the applicant to provide the official NIH identifier(s)for the hESC line(s)to be used in the proposed research. Applications that do not provide this information will be returned without review.

PUBLIC ACCESS TO RESEARCH DATA THROUGH THE FREEDOM OF INFORMATION ACT: The Office of Management and Budget (OMB) Circular A-110 has been revised to provide public access to research data through the Freedom of Information Act (FOIA) under some circumstances. Data that are (1) first produced in a project that is supported in whole or in part with Federal funds and (2) cited publicly and officially by a Federal agency in support of an action that has the force and effect of law (i.e., a regulation) may be accessed through FOIA. It is important for applicants to understand the basic scope of this amendment. NIH has provided guidance at http://grants.nih.gov/grants/policy/a110/a110_guidance_dec1999.htm.

Applicants may wish to place data collected under this initiative in a public archive, which can provide protections for the data and manage the distribution for an indefinite period of time. If so, the application should include a description of the archiving plan in the study design and include information about this in the budget justification section of the application. In addition, applicants should think about how to structure informed consent statements and other human subjects procedures given the potential for wider use of data collected under this award.

URLs IN NIH GRANT APPLICATIONS OR APPENDICES: All applications and proposals for NIH funding must be self-contained within specified page limitations. Unless otherwise specified in an NIH solicitation, Internet addresses (URLs) should not be used to provide information necessary to the review because reviewers are under no obligation to view the Internet sites. Furthermore, we caution reviewers that their anonymity may be compromised when they directly access an Internet site.

HEALTHY PEOPLE 2010: The Public Health Service (PHS) is committed to achieving the health promotion and disease prevention objectives of "Healthy People 2010," a PHS-led national activity for setting priority areas. This RFA is related to one or more of the priority areas.

Potential applicants may obtain a copy of "Healthy People 2010" at http://www.health.gov/healthypeople.

AUTHORITY AND REGULATIONS: This program is described in the Catalog of Federal Domestic Assistance No. Nos. 93.846 and is not subject to the intergovernmental review requirements of Executive Order 12372 or Health Systems Agency review. Awards are made under authorization of Sections 301 and 405 of the Public Health Service Act as amended (42 USC 241 and 284) and administered under NIH grants policies described at http://grants.nih.gov/grants/policy/policy.htmand under Federal Regulations 42 CFR 52 and 45 CFR Parts 74 and 92.

The PHS strongly encourages all grant recipients to provide a smoke-free workplace and discourage the use of all tobacco products. In addition, Public Law 103-227, the Pro-Children Act of 1994, prohibits smoking in certain facilities (or in some cases, any portion of a facility) in which regular or routine education, library, day care, health care, or early childhood development services are provided to children. This is consistent with the PHS mission to protect and advance the physical and mental health of the American people.

Return to Volume Index
Return to NIH Guide Main Index